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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/797,019	03/11/2004	Bradley A. Saville	27462	3927

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MANELLI DENISON & SELTER
2000 M STREET NW SUITE 700
WASHINGTON, DC 20036-3307

EXAMINER	
GOUGH, TIFFANY MAUREEN	
ART UNIT	PAPER NUMBER
1657	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/797,019	SAVILLE ET AL.	
	Examiner	Art Unit	
	Tiffany M. Gough	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-16,19 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-16,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed 10/19/2006 has been received and entered into the case. Claims 1-7,9-16,19,20 are pending and have been considered on the merits. All arguments and amendments have been considered.

Oath/Declaration

The petition decision granted under 37 CFR1.47(a) , submitted 11/18/2004, has been received and admitted into the case.

Information Disclosure Statement

The information disclosure statement filed 3/11/2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7,9-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Particularly claim 1 and its dependent claims are confusing and fails to distinctly claim applicants invention because, it reads, " a method of enhancing the... activity of an enzyme to a substrate susceptible to said enzyme..." It appears as if steps or words have been eliminated from the method as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3,6,7,10,19,20 are/stand rejected under 35 U.S.C. 102(b) as being anticipated by Bailey et al (US 4,204,041,1980).

Applicant claims a method of enhancing the intrinsic activity of an enzyme solution, preferably a hydrolase such as amylase and glucoamylase, by treating with a purifying agent, activated carbon. The raw enzyme solution is diluted with wither water or an aqueous buffer solution. The enzyme to carbon ratio is not to exceed 50:1.

Bailey et al teach the use of activated carbon to immobilize and stabilize enzymes. They teach many advantages of using activated carbon with enzymes , specifically its acceptance as an absorbent for the removal of trace impurities from liquids therefore protecting enzymes from poisoning by metals or impurities in industrial process mixtures by absorbing the impurities before penetrating (see col.4,lines 39-46). They specifically teach the use of activated carbon with hydrolases, specifically glucoamylase and amylase. During the immobilization process, Bailey disclose the purification of the enzyme product which demonstrate excellent stability and extended enzyme lifetime. Further, they disclose the importance and value of the intimate combination of activated carbon and the enzymes catalytic activity (see col. 5lines 45

continued to col. 6 lines 30). They further display enzyme to carbon ratio's of 45:1, 42:1, and 43:1 (see table in col.9). Bailey et al further teach diluting the enzyme solution in an aqueous buffer and then treating the enzyme solution with the purifying agent (see col. 10, lines 10-12).

The above claims stand rejected under 102(b).

Applicant's arguments filed 10/19/200 have been fully considered but they are not persuasive because applicant argues that Bailey discloses an enzyme which is attached to the activated carbon and wherein the bound material must be present in the medium when the reaction takes place. Further, applicant states that their invention does not involve an enzyme bound to an agent. They further state that Bailey does not disclose a reason for dilution. They further ague that applicant invention is distinct from Bailey because applicants enzyme is removed from the activated carbon before it is used. While these arguments have been considered, they are not persuasive because, applicant's method merely comprises diluting a raw enzyme solution with an aqueous solution and treating with a purifying agent for a period of time. Removal of the enzyme from the activated carbon prior to use is not recited in the claims nor is the whether or not the enzyme is bound, thus the argument is not commensurate in scope. The method as claimed is taught by Bailey thus the reference anticipates the claimed subject matter.

Claims 1-6,9,19,20 are/stand rejected under 35 U.S.C. 102(b) as being anticipated by Lausten et al (US2002/0020668 A1).

Applicant claims a method of enhancing the intrinsic activity of an enzyme solution, preferably a hydrolase such as amylase, glucoamylase and cellulase, by treating with a purifying agent, activated carbon. The raw enzyme solution is diluted with wither water and removed by filtration. Such method may also be carried out through a column. The enzyme to carbon ratio is not to exceed 50:1, preferably 15:1.

Lausten teach the use of activated carbon in a fermentation broth, particularly with enzymes such as amylases and cellulases, to remove soluble impurities by purification improving the quality of a product (see abstract and 0015,0018-0046). The carbon is added at concentration of up to 2% w/w (see 0046). The enzyme solutions are further diluted with water before addition of carbon and further microfiltered (see examples 1 and 2), although they also teach the purification of such enzyme solutions with activated carbon may also be performed by such methods such as ultrafiltration, chromatographic methods, i.e. column method, adsorption and/or crystallization (see 0057).

Although the above references do not specifically state the enhancement of the enzyme activity, the method of treating an enzyme solution with a purifying agent, activated carbon, is the same, and further it is known in the art that activated is a purifying agent of enzymes and by purifying a substance one is further enhancing its intrinsic properties/activites, therefore, the enhancement of activity must be an inherent property of mixing such solutions together.

The above claims stand rejected under 102(b).

Applicant's arguments filed 10/19/200 have been fully considered but they are not persuasive because applicant argues that Lausten discloses dilution of an enzyme solution with water at an upper ratio, while this may be true, applicant merely claims diluting the enzyme solution with at least two parts of an aqueous solution. The dilution taught by Lausten is at least two parts dilution, thus the reference anticipates this limitation. Applicant argues that the method taught by Lausten would not necessarily lead to an enhanced enzyme activity. However, as previous stated the method of treating an enzyme solution with a purifying agent, activated carbon, is the same, and further it is known in the art that activated is a purifying agent of enzymes and by purifying a substance one is further enhancing its intrinsic properties/activites, therefore, the enhancement of activity must be an inherent property of mixing such solutions together. Thus, applicants arguments fail to be persuasive and the rejection stands.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12,13 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shenoy et al (J. of Bioscience, vol 7, 1985) in view of http://www.ap-lab.com/circular_dichroism.htm and Lausten et al (US2002/0020668 A1).

Applicant claims a method of enhancing the intrinsic activity of an enzyme solution by treating with a purifying agent. The enzyme solution of enhanced activity is claimed to have a relative absorbance intensity lower than the raw enzyme solution, preferably in the CD spectral range of 205-230 nm. Applicant further claims the enzyme to be alpha-amylase.

Shenoy et al (J. of Bioscience, vol7,1985) teach the purification of glucoamylases. They teach that the catalytic activity of a protein, i.e. enzyme is related to its "active" conformation, i.e. secondary and tertiary structure. The specific activity of the purified enzymes was three times higher than that of the original non-purified glucoamylase (see p.400). They teach that the UV (CD) spectra of glucoamylases from 3 species show peaks at 289-293,279-282 and 257-259 nm (see p.400-402), but also reveal negative bands at 217-220,208-210 (see p. 402).

Shenoy does not teach lower CD spectrum ranges such as those claimed by applicant nor alpha-amylase.

Information found at http://www.ap-lab.com/circular_dichroism.htm teaches that any change in structure of proteins will affect the CD spectral range, therefore a change in the spectral range appears to be an inherent property of purification, i.e, structural change, of a protein. Thus, one of ordinary skill in the art would be motivated and it would therefore be obvious to claim a CD spectral range lower than that of a raw enzyme solution given that a change in structure ultimately affects the CD spectrum. When purifying a protein such as enzymes, one would have a reasonable expectation of success in obtaining a CD spectrum range lower than that of the raw enzyme solution

given that purification ,enhancing the catalytic activity of an enzyme, ultimately alters the secondary and tertiary structure, therefore altering the CD spectrum range. Further, it would be obvious to optimize these parameters through routine experimentation.

Also it would be obvious to use other hydrolase enzyme such as alpha-amylase because Lausten teach the use of activated carbon in a fermentation broth, particularly with enzymes such as amylases and cellulases, to remove soluble impurities by purification improving the quality of a product (see abstract and 0015,0018-0046). Therefore, one of ordinary skill in the art at the time of the invention would have been motivated to purify an enzyme such as alpha-amylase with activated carbon as taught by Lausten and would have a reasonable expectation of success in obtaining a CD spectral range lower than that of the raw enzyme solution given what is known in the art of the change in structure by purification of a protein.

The above claims stand rejected under 103(a).

Applicant's arguments filed 10/19/200 have been fully considered but they are not persuasive because applicant argues that one cannot use changes in CD spectrum to develop a process or to predict how a treatment would lead to a specific change in activity, therefore it is unclear how applicant is using their CD spectral results in regards to applicants invention. Further, applicant admits that they like Shenoy use CD to examine changes in structure following enzyme treatment/processing, thus applicants arguments appear to be moot. However, applicant states that they do not claim a specific CD spectra, but rather that their process leads to a change in structure as supported by CD. Applicant absolutely claims a specific CD spectra in claims 12-15,

thus applicant arguments are not supported by the claims. Further they argue against the Alliance reference but then further admit that Alliance shows CD as a tool to show structural changes following a process, which is what applicant states they are using CD for as well. Thus, the arguments are not persuasive and the rejection stands.

Claims 1-3,5,10,11,14 ,19, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aikat et al (Biotechnology Letters, vol 23, 2001,p.295-301) in view of Bailey et al (US 4,204,041,1980) or Lausten et al (US2002/0020668 A1).

Applicant claims a method of enhancing the intrinsic activity of an enzyme solution, specifically a hydrolase, by treating with a purifying agent, activated carbon, and further removing the activated carbon from the enzyme solution by centrifugation. The purified enzyme solution is said to have a CD and UV distinct from that of the raw enzyme solution, specifically 30 nm less and the enzyme to carbon ratio is not to exceed 15:1.

Aikat et al teach the purification of protease by activated charcoal, i.e. activated carbon. They demonstrate the purification by activated charcoal in terms of fold purification and by electrophoretic analysis (see introduction). The enzyme solution was mixed with activated charcoal and allowed to react for a specific period of time prior to centrifugation, thus removing the activated carbon, at which time the supernatant was examined by spectroscopy. Further analysis was carried out by electrophoresis (see p. 296). The enzyme solution (1 ml) was treated with 50 to 150 mg of activated charcoal, although 75 mg of charcoal was selected as their optimum ratio. By gel analysis they

observed the removal of almost all of the smaller proteins, confirming the purifying action of activated charcoal.

Further, Aikat diluted the crude enzyme solution 10 times to bring it's absorbance within the range of that of charcoal-treated enzyme, which shows distinct troughs at 260 nm and a peak at 280nm. In the crude diluted solution there appeared to be a peak at 260 nm and no valley (see p.299 to 300).

Aikat does not teach diluting the raw enzyme solution prior to treating with a purifying agent.

However, as stated above both Bailey and Lausten teach diluting an enzyme solution prior to treating the activated carbon. Thus , at the time of the invention it would have been obvious to one of ordinary skill in the art to dilute an enzyme solution prior to treatment because the prior art teaches dilution prior to treatment with activated carbon. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to have diluted an enzyme solution prior to purification with activated carbon with a reasonable expectation for successfully enhancing the intrinsic activity of such solution because the art teaches such success when using the claimed enzyme solution and purifying agent.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tiffany M. Gough whose telephone number is 571-272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tiffany Gough

RUTH DAVIS
PRIMARY EXAMINER